FIG. 1

peptide selection

peptide optimization

formation of Fc-peptide DNA construct

insertion of construct into expression vector

transfection of host cell with vector

expression of vector in host cell

Fc multimer formation in host cell

isolation of Fc multimer from host cell-

FIG. 3A Fc

FIG. 3B

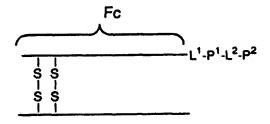
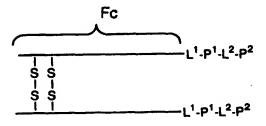
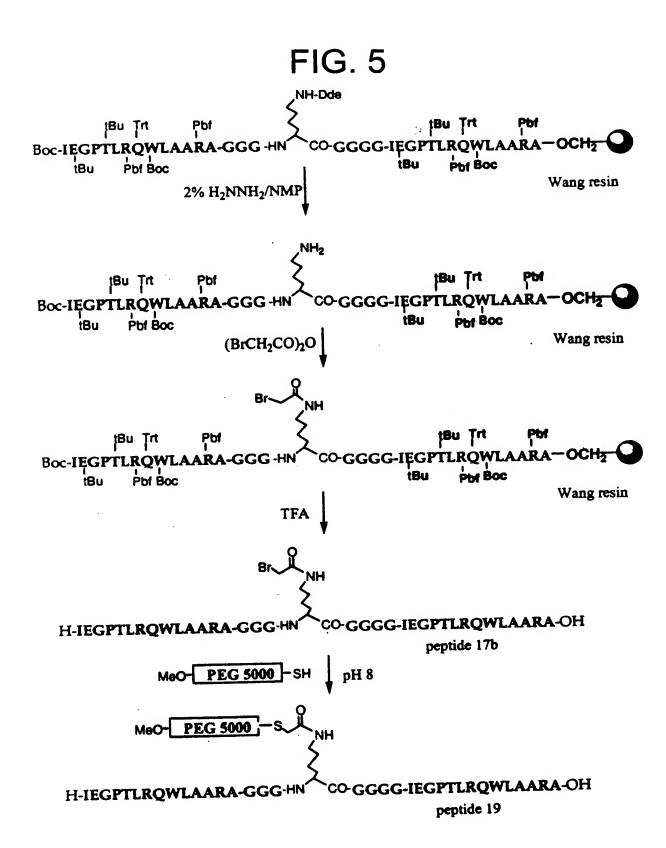


FIG. 3C



	•	AIG	SACA	MAC	ICA		416		4CC.	LIG		166	دررر	30 M.	ec re	CTO	بحصر	GGA	CCG	TCA	
	1	TAC	CTGT	TTG	AGT	GTG:	raca	\GG7	rggi	AAC?	AGG	rcg <i>i</i>	AGGG	CTI	rga(GAC	ccc	CCT	'GGC	AGT	60
a		M I	о к	T	н	T	С	P	P	С	P	A	P	E	L	L	G	G	P	3	•
	61	GTC	rtcc	CTT	ccc	CCC	AAA					CT		SATO	TCC	CGC	ACC	CCI	'GAG		120
	0.1	CAG	AAGG?	GAA	GGG	GGG:	rTT?					•		CTAC	GAGC	GCC	TGC	GGA	CTC		120
a.		V I	F L	F	P	P	K	P	K	D	T	L	M	I	s	R	T	P	E	V	-
	121		rgcgi	rggt	GGT	GGA	CGT	AGG	CA	_		CC	_			TTC		TGC	TAC		180
	121		ACGC/	ACCA	CCA	CCT	GCAC	CTC	GT(•			•	ACC	ATG		100
a		т	c v	V	v	D	V	S	H	E	D	P	E	V	K	F	N	W	Y	V	•
	101	GAC	GGCG	rgga	GGT	GCA'											TAC				240
	181	CTG	CCGC	ACCT	CCA	CGT	-							-						-	240
a		D C	g v	E	v	н	N	A	K	T	ĸ	P	R	E	E	Q	Y	N	S	T	•
		TAC	CGTG:	rggt	CAG	CGT	CCT		_					CTG	CT	GAA?	rgg	CAAC	GAC	TAC	200
	241	ATG	GCAC	ACCA	GTC	GCA	GGA					GGT		GAC	CGA	CTT	ACC	STT	CTC	ATG	300
a		Y . :	R V	v	s	v	L	T	V	L	н	Q	D	W	L	N	G	ĸ	E	Y	•
	201	AAG	TGCA	AGGT	CTC	CAA	CAA	AGC	CCT	ccc.	AGC	CCC	CAT	CGA	GAA	AAC	CATO	CTC	CÀA	AGCC	360
	301	TTC	ACGT	CCA	GAG	GTT	GTT	rcg	GGA	GGG	rcg	GGG	GTA	GCT	CTT	TTG	GTA(GAG	STTI	rcgg	300
a		K	C K	v	s	N	K	A	L	P	A	P	I	E	K	T	I	S	ĸ	A	-
	261	AAA	GGGC	AGÇC	CCG															SACC	420
	361	TTT	CCCG	rcgg	GGC																420
a		K	G Q	P	R	E	P	Q	V	Y	T	L	P	P	S	R	D	E	L	T	-
	421	AAG	AACC.	AGGT	CAG	CCT	GAC	CTG	CCT	GGT	CAA	AGG	CTT	CTA	TCC	CAG	CGA	CAT	CGC	CGTG	480
	421	TTC	TTGG	TCCA	GTC	GGA	CTG	GAC	GGA	CCA	GTT	TCC	GAA	GAT	AGG	GTC	GCT	GTA(GC G(CAC	
a		K	N Q	v	3	L	T	С	L	V	K	G	F	Y	P	3	D	I	A	V	•
	481	GAG	TGGG	AGAG	CAA	TGG	GCA	GCC	GGA	GAA	CAA	CTA	CAA	GAC	CAC	GCC'	TCC	CGT	GCT(GGAC	540
	401	CTC	ACCC	TCTC	GTT	ACC	CGT	CGG	CCT	CTT	GTT	GAT	GTT	CTG	GTG	CGG.	AGG	GCA	CGA	CCTG	
a		E	w e	S	N	G	Q	P	E	N	N	Y	K	T	T	P	P	V	L	D	•
	541	TCC	GACG	GCTC	CTT	CTT	CCT	CTA	CAG	CAA	GCT +··	CAC	CGT	GGA	CAA	GAG	CAG	GTG	GCA	GCAG	600
	741	AGG	CTGC	CGAG	GAA	GAA	GGA	GAT	GTC	GTT	CGA	GTG	GCA	CCT	GTT	CTC	GTC	CAC	CGT	CGTC	
a			D G																		
	601		AACG	+ -			+				+			-+-			+		• • •	• • • •	900
	501	CCC	TTGC	AGA	GAG	TAC	GAG	GCA	CTA	CGT	ACT	CCG	AGA	CGT	GTT	GGT	GAT	GTG	CGT	CTTC	
a		G	N V	P	S	С	3	V	M	Н	E	A	L	Н	N	H	Y	T	Q	K	•
	661		CTCT							684											
	301	TCC	GAGA	.GGG/	CAC	AGG	ccc	ATT													



TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS INVENTORS: FEIGE, et al.

APPLN. NO: A-527D

		XbaI	
c	1	TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCTGTTTTGAGTGTACAG M D K T H T C P	
c	61	CACCTTGTCCAGCTCCGGAACTCCTGGGGGGACCGTCAGTCTCCTCTTCCCCCCAAAAC GTGGAACAGGTCGAGGCCTTGAGGACCCCCCTGGCAGTCAGAAGGAGAAGGGGGGTTTTG P C P A P E L L G G P S V F L F P P K P	20
c	121	CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA GGTTCCTGTGGGAGTACTAGAGGGGCCTGGGGACTCCAGTGTACGCACCACCACCACCTGCACT K D T L M I S R T P E V T C V V V D V S	
c	181	GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATG CGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC H B D P E V K F N W Y V D G V E V H N A	
c	241	CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCA GGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAGTCGCAGGAGT K T K P R E E Q Y N S T Y R V V S V L T	
c	301	CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG GGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGTTCCAGAGGTTGTTTC V L H Q D W L N G K E Y K C K V S N K A	
c	361	CCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC GGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTGGTG L P A P I E K T I S K A K G Q P R E P Q	
c	421	AGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT TCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGA V Y T L P P S R D E L T K N Q V S L T C	80
c	481	GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC CGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCGTCG L V K G F Y P S D I A V E W B S N G Q P	
c	541	CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT GCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGGAGA E N N Y K T T P P V L D S D G S F F L Y	
c	601	ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG TGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGC S K L T V D K S R W Q Q G N V F S C S V	
C	661	TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTA ACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT M H E A L H N H Y T Q K S L S L S P G K	
c	721	AAGGTGGAGGTGGTATCGAAGGTCCGACTCTGCGTCAGTGGCTGGC	
		BamHİ I	
	781	AATCTCGAĞGATCC 794 TTAGAGCTCCTAGG	

FIG 8

	X	aI								1	1	-	•	J							
	1			+			4	 -	·		+			+				+		ATGTC	60
c		AGAT	CTA	RAC.	RAA.	ATT	3A'1"	(AA)	M	CTC	CT	TATT	GT							TACAG C P	
	61			+		 .	1		. .		+			+				+		AAAAC TTTTG	120
c		Б	С	P	A	P	E	L	L	G	G	P	S	٧	F	L	F	P	P		•
c	121	GGTT	CCT	+ GTG(GGA(GTAC	CTAC	AG	GCC	CTGC	GG/	CTC	CAC	+ GTG	race	 GCA	CCA	+	CCT	GCACT	
	101																			TAATG	
c	181		GCT.	CTC	GGG/	ACTO	CCAC	TT	CAAC	TTC	GACC		CAC	CTO	3CC	GÇA	CCT	CCA		ATTAC N A	
	241			+		• • • •	1	 -	• • •		+		• •	• • +	• • •		• • •	+••	• • •	CCTCA GGAGT	300
c					-				_				_					_		L T	•
c	301	GGCA	GGA	CGT	GGT	CCTO	GACC	CGAC	CTT	ACC	TTC	CTC	ATC	GTT(CAC	GTT	CCA	GAG	GTT	GTTTC K A	
	361			+		 .	1	 -	· · ·	· ·	+	• • •		+	• • •			+	• • •	ACCAC TGGTG	420
C		L	P	A	P	I	E	K	T	I	3	K	A	K	G	Q	P	R	E	P. Q	•
С	421	TCCA	CAT	+ GTG(GGA	CGG/	 3GG1	rag(GCC	CTI	++·		TG	· · + GTT	 CTT	GGT	CCA	+ · ·	GGA	GACCT CTGGA T C	480
	481	CGGA	CCA	TT.	rcc	GAAC	GAT	AGG(GTC	CTC	TAC	CGG	CAG	··+	CAC	CCT	CTC	GTT	ACC	GCAGC CGTCG	540
С		CGGA	GAA	CAA	CTA	CAAC	GACC	CAC	3CC1	rcc	CGT		GA	CTC	CGA	CGG	CTC	CTT	CTT	CCTCT	
c	241			GTT	GAT		CTGC	TG	CGG	AGG	CAC		CT	GAG	CT	GCC	GAG	GAA	GAA	GGAGA L Y	
c	601	TGTC	GTT	CGA	GTG	GCAC	CTC	TT	CTC	TCC	CAC	GTC	GT	+ CCC	CTT	 GCA	GAA	GAG	TAC	CTCCG GAGGC S V	660
•		TGAT	GCA'	rgac	GGC'	rcto	GCA (CAAC	CAC	CTAC	CAC	CAG	AA	GAG	CT	CTC	CCI	GTC	TCC	GGGTA	
c	991	ACTA	CGT	ACTY	CCG	AGAC	CGTC	TT	GT(SATO	TGC	GTC	TT	CTC	GGA	GAG	GGA	CAG	AGG	CCCAT G K	
	721	TTCC	ACC	rcc.	ACC	ACC	ATAC	··· CT	rcci	AGG	·+· CTG/	AGAC	GC	··+ Agt	CAC	CGA	CCG	ACC	λGC	TGCTG ACGAC	
c		GTGG'	TGG	AGG'	TGG	CGG	CGG	AGG'	rat'	rgac	GGG	CCA	AC	CCT	TCG	CCA	ATG	GCI	TGC	A G	
c	181	CACC	ACC'	TCC	ACC	GCC	GCC?	rcc.	ATA	ACTO	CCC	GGT	TG	GGA	AGC	GGT	TAC	CGA	LACG	TCGTG A R	
					8	amH:	I														

GCGCATAATCTCGAGGATCCG 841 CGCGTATTAGAGCTCCTAGGC c

FIG. 9

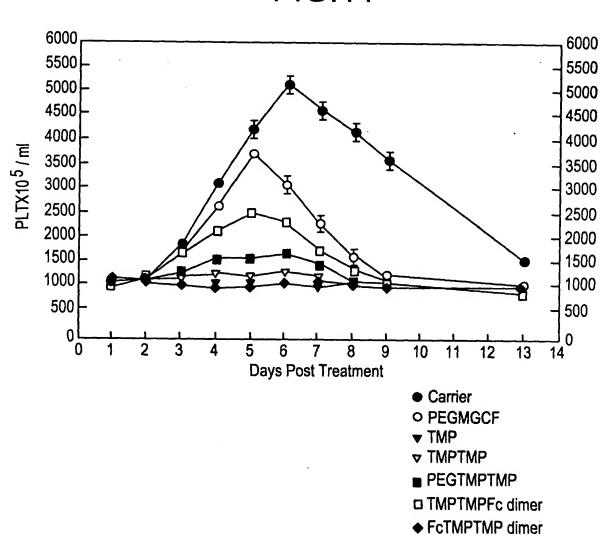
		XbaI								•			•									
c	1	TCTA		+	• • •	• • • •	• • • •		· • • ·	• • • •	+-	· - · -		ATA	CTAC	CT	TCC	+ AGG		AGAC	+	
c	61	GTCA	CAC	- · + CGA	CCG	ACG	AGC	L	ACC		VCC1	 ACCG	CC'	rcc(ccci	ACC	GTA	+··			+ T	120
c	121	GGGA		GT	TAC	CGA	ACG:	rcg	rgc	 GCG1	rcc	CCT	CC	GCC	ACC	 CT	GTT	+ TTG	AGT		+ 'A	180 -
c	181	GTCC: CAGG		AAC	GGG		rgg	CT	rgac	GAC	CCC		GG	CAG	CA	AAA	GGA	Gλλ		GGGT	+	
c	241	TTGG	GTT	··+ CCT	 GTG	GGA	GTAC	TAC	GAG	GCC	+ TG	GGA	CT	+ CCA	STG:	 TAC	GCA	CCY	CCA	• • • •	+ iC	300
c	301	TGAG	GGT	··+ GCT	rct(GGG	ACT	CAC	GTT(CAAC	+ TTC	GACC	AT	- · + GCA	CT	GCC	GCA	+ CCT	CCA	• • • •	+ T	
c	361	TACG	• • • •	+ CTGʻ		CGG	CGC	+ ·	CCT	CGTC	+-	STTC	TC	+ GTG	CAT	GGC	 ACA	+	GTC		+ G	
c	421	AGTG	GCA(+ GGA	CGT	 GGT(CCT	GAC	CGA	CTT	. + - ACC	GTTC	CT	+ Cate	 GTT	CAC	GTT	+	GAG		+ T	
С	481	TTCG		+	TCG		GTA(GCT(CTT	TTG	+- GTA		TT	rcg	GTT	rcc	CGT	cgg	GGC	TCTT	+	
c	541	CACA GTGT		+ Cat	GTG	GGA	CGG	+ GGG'	TAG	GGC	- + <i>-</i> :CT:	• • • •	GA	··+ CTG	GTT	CTT	GGT	+	GTC	GGAG	+	600 -
c	601	CCTG GGAC C	GGA	+ CCA	GTT	TCC	GAA	+ Gat	AGG	CTC	- + - 3CT(GTAC	 GG	+ GCA	CCT	CAC	CCT	+	GTT		G:	
c	661	AGCC TCGG	CCT	+ CTT	CTT	GAT	GTT	+ CTG	GTG	CGGI	+ + - AGG	GCAC	GA	+ CCT	GAG	GCT	GCC	GAG	GAA		. + 3G	
c	721	TCTA AGAT Y	GTC	+ GTT	CGA	GTG	GCA	+ CCT	GTT	CTC	- + - GTC	CAC	GT	··+ CGT	CCC	CTT	GCA	GAA	GAG	• • • •	· +	
c	781	CCGT GGCA V	CTA	+ CGT	ACT	CCG	AGA	+ · · CGT	OTT	GGT	- + - GAT	GTG	 CGT	··+ CTT	CTC	GGA	GAG	+ GG≀	CAG		- + 	
			Ba	mHI																		

K *

C

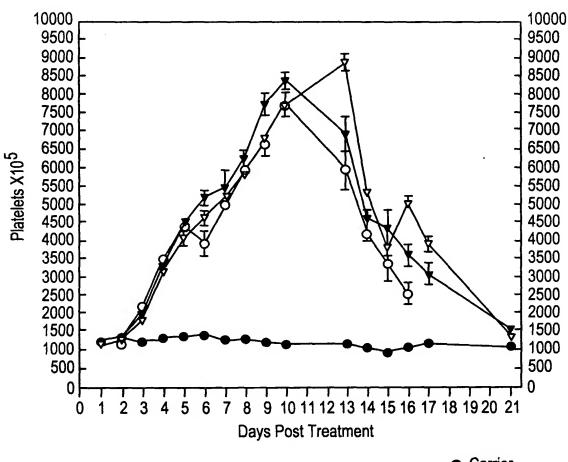
	,	Xbai	
	1	TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGATCGAAGGTCCGACTCTGC	50
c		AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACTAGCTTCCAGGCTGAGACG M I E G P T L R	
	61	GTCAGTGGCTGGCTGGTGCTGGTGGAGGCGGTGGGGACAAAACTCACACATGTCCAC	
c	01	CAGTCACCGACGAGGAGCACGACCACCCCCGCTGTTTTGAGTGTGTACAGGTG Q W L A A R A G G G G D K T H T C P P	
	121	CTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCCTCTTCCCCCCAAAACCCA	
С	121	GAACGGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGGAGAAGGGGGGTTTTGGGT C P A P E L L G G P S V F L F P P K P K	
	101	AGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCC	240
c	101	TCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCACCTGCACTCGG D T L M I S R T P E V T C V V D V S H	
	241	ACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCA	300
c	441	TGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTACGGT E D P E V K F N W Y V D G V E V H N A K	
	301	AGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCG	360
c	301	TCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAGTCGCAGGAGTGGC T R P R E B Q Y N S T Y R V V S V L T V	
		TCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCC	4 2 0
c	361	AGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGTTCCAGAGGTTGTTTCGGG L H Q D W L N G K E Y K C K V S N K A L	4
		TCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGG	400
c	421	AGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTGGTGTCC PAPIEKTISKAKG QPREPQV	
	401	TGTACACCCTGCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCC	540
c	481	ACATGTGGACGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGACGG Y T L P P S R D E L T K N Q V S L T C L	
	E 4 1	TGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGG	600
c	541	ACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCGTCGGCC V R G F Y P S D I A V E W E S N G Q P E	
		AGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACA	560
c	601	TCTTGTTGATGTTCTGGTGCGGAGGGGGCACGACCTGAGGCTGCCGAGGAAGAAGAAGGAGATGT N N Y K T T P P V L D S D G S F F L Y S	
		GCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGA	720
C	661	CGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGCACT K L T V D K S R W Q Q G N V F S C S V M	
		TGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAAT	780
c .	721	ACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGGACAGAGGCCCATTTA H E A L H N H Y T Q K S L S L S P G K	
-		BamHI	
	70-	AATGGATCC	
	/81	1 ····· 789 TTACCTAGG	

FIG.11



APPLN. NO: A-527D

FIG.12



- Carrier
- o PEG MGDF
- ▼ TMPTMPFc dimer
- ▼ FcTMPTMP dimer

	Х	baI										_	- •	•							
	1	TCTA										ATA									C + 60
2		AGAT												ATA	CCT		TTG		GTG'		3
6		CACC'												AGT	CTT	CCT	CTT	CCC	CCC.	AAAA	3
3		GTGG. P																		TTTT(3
1.5		CCAA																			
:		CCTT	CCT	STG	GGA(GTA	CTAC	GAG	GCC	CTG	GGG.	ACTO	CAC	GTG	TAC	GCA	CCA	CCA	CCT		_
		GCCA																			
18	31	CGGT	GCT	CTC	GGG	ACTO	CCA	STT	CAAC	GTT(GAC	CATO	CAC	CCT	GCC	GCA	CCT	CCA	CGT		
2.4		CCAA																		_	A + 300
:	••	GGTT K	CTG	rrr(CGG	CGC	CCT	CTC	CGTY	CAT	GTT	GTC	STG	CAT	GGC.	ACA	CCA	GTC	GCA		r
30		CCGT																			G + 360
3		GGCA V					-										-			GTTT K	
		стссс																			+ 420
2		GGGA	GGG'	TCG(GGG	GTA(GCT	CTT	TTG	GTA(GAG	GTT	rcg	GTT	TCC	CGT	CGG	GGC	TCT		G
4.5		AGGT					_														r + 480
4. 3	6 1	TCCA	CAT	STG	GGA	CGG	GGG'	PAG	GGC	CCT	ACT	CGA	CTG	GTT	CTT	GGT	CCA	GTC	GGA		A
4.6	31	GCCT										CGC									C + 540
• • • • • • • • • • • • • • • • • • •		CGGA	v	ĸ	G	F	Y	P	S	D	I	A	٧	B	W	E	3	N	G	Q :	P -
54	11	CGGA		+			• • • •				-+-			+				+	• • •	• • • •	+ 600
3		E ACAG			_															L	
60)1	TGTC	 GTT	+ CGA	GTG	GCA	CCT	+ GTT(CTC	GTC	-+- Cac	CGT	CGT	ccc	CTT	GCA	GAA	GAG	TAC	GAGG	+ 660 C
3		S	K	L	T	V	D	K	3	R	W	Q	Q	G	N	V	F	3	С	S	٧ -
66	51	ACTA	 CGT	+ ACT	 CCG	AGA	CGT	+ GTT(GGT	GAT	·+· GTG	CGT	 CTT	··+ CTC	GGA	GAG	GGA	+ CAG	AGG	CCCA	+ 720 T
3		M	H	B	A	L	Н	N	H	Y	T	Q	K	S	L	3	L	3	P	G	к -
72	21	AAGG		+				+			-+-			+				+			+ 780
c		G	G	G	G	G	G	G	T	Y	S	С	H.	F	G	P	L	T	W	v	С -
										Bam	ΗŢ										
71	81	GCAA	• • •	+	• • •			+	• • •	• • •	-+-	- 8	12								
c		CGTT K			CCC			TAG	AGC	ACC	TAG	G									

FIG. 14 XbaI+ 60 c M G G T Y S C H -ACTTCGGCCGCTGACTTGGGTATGTAAGCCACAAGGGGGTGGGGGAGGCGGGGGGACA •+••••• 120 TGAAGCCGGGCGACTGAACCCATACATTCGGTGTTCCCCCACCCCCTCCGCCCCCCTGT F G P'L T W V C K P Q G G G G G D C AAACTCACACGTGCCCAGCCACCTGAACTCCTGGGGGGACCGTCAGTTTTCC TTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGG THTCPPCPAPELLGGPSVFL C TCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCG AGAAGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGC C PPKPKDTLMISRTPEVTC TGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG 300 ACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGC V V D V S H E D P E V K P N W Y V D G C TGGAGGTGCATAATGCCAAGACAAAGCCGGGGAGGAGCAGTACAACAGCACGTACCGTG 301 ------ 4360 EVHNAKTKPREEQYNSTYRVc TGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCA 361 -----+ 420 ACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGT c V S V L T V L H Q D W L N G K E Y K C K -AGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGC+ 480 TCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCG c V S N K A L P A P I E K T I S K A K G Q -AGCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCGGGATGAGCTGACCAAGAACC TCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGGTTCTTGG C PREPQVYTLPPSRDELTKNQ-**AGGTCAGCCTGACCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGG** TCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCC V S L T C L V K G F Y P S D I A V E W E -C **AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACG** TCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGC S N G Q P E N N Y K T T P P V L D S D G C GCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACG 661 -----+ 720 CGAGGAAGAAGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGC S F F L Y S K L T V D K S R W Q Q G N V C TCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT 721 -----+ 780 AGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGA F S C S V M H E A L H N H Y T Q K S L S c BamHI

c

TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS

INVENTORS: FEIGE, et al. APPLN. NO: A-527D

FIG. 15 XbaI ь MGGTYSC CCACTTCGGCCCACTGACTTGGGTTTGCAAACCGCAGGGTGGCGGCGGCGGCGGCGGCGGTGG GGTGAAGCCGGGTGACTGAACCCAAACGTTTGGCGTCCCACCGCCGCCGCCGCCACC b H F G P L T; W V C K P Q G G G G G G TACCTATTCCTGTCATTTTGGCCCGCTGACCTGGGTATGTAAGCCACAAGGGGGTGGGGG 121 ------+-----+ 180 ATGGATAAGGACAGTAAAACCGGGCGACTGGACCCATACATTCGGTGTTCCCCCACCCCC ь TYSCHFGPLTWVCKPQGGGG AGGCGGGGGGACAAAACTCACACATGTCCACCTTGCCCAGCACCTGAACTCCTGGGGGG TCCGCCCCCCTGTTTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCCCC b GGGDKTHTCPPCPAPELLGG ACCGTCAGTTTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCC TGGCAGTCAAAAGGAGAAGGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGG PSVFLFPPKPKDTLMISRTP b TGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTG ACTCCAGTGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGAC EVTCVVVDVSHEDPEVKFNW ь GTACGTGGACGCGTGGAGGTGCATAATGCCAAGACAAGCCGCGGGAGGAGCAGTACAA CATGCACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCCTCCTCGTCATGTT ь YVDGVEVHNAKTKPREEQYN CAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAA GTCGTGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTT ь STYRVVSVLTVLHQDWLNGK-GGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTC CCTCATGTTCACGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAG b EYKCKVSNKALPAPIEKTIS CAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGA 541 -----+ 600 GTTTCGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACT þ KAKGQPREPQVYTLPPSRDE-GCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACAT 601 -----+ 660 CGACTGGTTCTTGGTCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTA LTKNQVSLTCLVKGFYPSD·I b CGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGT 661 -----+ 720 GCGGCACCTCACCCTCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCA AVEWESNGQPENNYKTTPPVь GCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTG CGACCTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCAC LDSDGSFFLYSRLTVDKSRW ь GCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACAC CGTCGTCCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTG Q Q G N V F S C S V M H E A L H N H Y T ь BamHI GCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATAATGGATCC

CGTCTTCTCGGAGAGGGGACAGAGGCCCATTTATTACCTAGG

OKSLSLSPGK*

b

		Par FIG. 10	
	•	 CTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGT	
c	1	AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCTGTTTTGAGTGTGTACA M D K T H T C	.G
	61	CACCTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCCTCTTCCCCCCAAAA	C + 120
C		TTGGD3D3AAAGGAGACTC3C3C3CAGTCAAAAGGAGAGAGGGGGTTTT P C P A P B L L G G P 3 V F L P P R	'G
	121	CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTG ***CCTCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGACCACCACCACCACCACCACCACCACCACCACCACCA	+ 180
C		K D T L M I S R T P E V T C V V D V 3CCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGAGGGGGGGG	_
c	181	CGCTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTA H E D P B V K F N W Y V D G V E V H N	+ 240 C
	241	CAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTC	+ 300
c		GGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAGTCGCAGGAG K T K P R E E Q Y N S T Y R V V S V L	T·
c	301	CGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGATCTCCAACAAA GGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGTTCCAGAGGTTGTTT V L H Q D W L N G K E Y K C K V 9 N K	+ 360
c	361	CCTCCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCA GGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTGGT L P A P I E K T I S K A K G Q P R E P	+ 420
	421	AGGTGTACACCCTGCCTCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACC	+ 480
c		V Y T L P P S R D E L T K N Q V S L T CCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAAGGAA	C -
c	481	GGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCGTC	+ 540
c	541	GGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTC CCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGGAG BNNYKTTPPVLDBGGCGCGCGCGACGACGACGA	+ 600 A
	601	ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGGAACGTCTTCTCATGCTCC	:G + 660
c		NGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGG SKLTVDKSRWQQGNVFSCS	V -
c	661	NGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGI NCTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGGCAGAGGCCCA M H E A L H N H Y T Q K S L S L S P G	+ 720
c	721	AGGTGGAGGTGGTGGCGGAGGTACTTACTCTTGCCACTTCGGCCCACTGACTTGGGTT TCCACCTCCACCACCGCCTCCATGAATGAGAACGGTGAAGCCGGGTGACTGAACCCAA G G G G G T Y S C H F G P L T W V	+ 780 LA
-	781	CAAACCGCAGGGTGGCGGCGGCGGCGGCGGTGGTACCTATTCCTGTCATTTTGGCCCC	SC + 840 SG
c		RPQGGGGGGGTYSCHFGP BamHI	. -

TGACCTGGGTATGTAAGCCACAAGGGGGTTAATCTCGAGGATCC ACTGGACCCATACATTCGGTGTTCCCCCAATTAGAGCTCCTAGG
T W V C K P Q G G *

C

TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS

INVENTORS: FEIGE, et al. APPLN. NO: A-527D

FIG. 17A

[<u>Aat</u>II sticky end] (position #4358 in pAMG21)

- GCGTAACGTATGCATGGTCTCC
- 3' TGCACGCATTGCATACGTACCAGAGG-
- -CCATGCGAGAGTAGGGAACTGCCAGGCATCAAATAAAACGAAAGGCTCAGTCGAAAGACT --GGTACGCTCTCATCCCTTGACGGTCCGTAGTTTATTTTGCTTTCCGAGTCAGCTTTCTGA -
- -GGGCCTTTCGTTTATCTGTTGTTGTCGGTGAACGCTCTCCTGAGTAGGACAAATCCGC--CCCGGAAAGCAAAATAGACAACAACACCCACTTGCGAGAGGACTCATCCTGTTTAGGCG-
- CGGGAGCGGATTTGAACGTTGCGAAGCAACGCCCGGAGGGTGGCGGGCAGGACGCCCGC GCCCTCGCCTAAACTTGCAACGCTTCGTTGCCGGGCCTCCCACCGCCCGTCCTGCGGGCG -
- CATAAACTGCCAGGCATCAAATTAAGCAGAAGGCCATCCTGACGGATGGCCTTTTTGCGT GTATTTGACGGTCCGTAGTTTAATTCGTCTTCCGGTAGGACTGCCTACCGGAAAAACGCA -

AatII

- TTCTACAAACTCTTTTGTTTATTTTTCTAAATACATTCAAATATGGACGTCGTACTTAAC AAGATGTTTGAGAAAAAAAAAAAAAAAAGATTTATGTAAGTTTATACCTGCAGCATGAATTG -
- TTTTAAAGTATGGGCAATCAATTGCTCCTGTTAAAATTGCTTTAGAAATACTTTGGCAGC AAAATTTCATACCCGTTAGTTAACGAGGACAATTTTAACGAAATCTTTATGAAACCGTCG -
- GGTTTGTTGTATTGAGTTTCATTTGCGCATTGGTTAAATGGAAAGTGACCGTGCGCTTAC CCAAACAACATAACTCAAAGTAAACGCGTAACCAATTTACCTTTCACTGGCACGCGAATG -
- TACAGCCTAATATTTTTGAAATATCCCAAGAGCTTTTTCCTTCGCATGCCCACGCTAAAC ATGTCGGATTATAAAAACTTTATAGGGTTCTCGAAAAAGGAAGCGTACGGGTGCGATTTG -
- GATAATTATCAACTAGAGAAGGAACAATTAATGGTATGTTCATACACGCATGTAAAAATA CTATTAATAGTTGATCTCTTCCTTGTTAATTACCATACAAGTATGTGCGTACATTTTAT -
- AACTATCTATATAGTTGTCTTTCTCTGAATGTGCAAAACTAAGCATTCCGAAGCCATTAT TTGATAGATATATCAACAGAAAGAGACTTACACGTTTTGATTCGTAAGGCTTCGGTAATA -
- TAGCAGTATGAATAGGGAAACTAAACCCAGTGATAAGACCTGATGATTTCGCTTCTTTAA ATCGTCATACTTATCCCTTTGATTTGGGTCACTATTCTGGACTACTAAAGCGAAGAAATT -
- TTACATTTGGAGATTTTTTATTTACAGCATTGTTTTCAAATATATTCCAATTAATCGGTG AATGTAAACCTCTAAAAAATAAATGTCGTAACAAAAGTTTATATAAGGTTAATTAGCCAC -
- AATGATTGGAGTTAGAATAATCTACTATAGGATCATATTTTATTAAATTAGCGTCATCAT TTACTAACCTCAATCTTATTAGATGATGATATCCTAGTATAAAATAATTTAATCGCAGTAGTA -
- AATATTGCCTCCATTTTTTAGGGTAATTATCCAGAATTGAAATATCAGATTTAACCATAG TTATAACGGAGGTAAAAAATCCCATTAATAGGTCTTAACTTTATAGTCTAAATTGGTATC -
- AATGAGGATAAATGATCGCGAGTAAATAATATTCACAATGTACCATTTTAGTCATATCAG-- TTACTCCTATTTACTAGCGCTCATTTATTATAAGTGTTACATGGTAAAATCAGTATAGTC -

- -GCAAGTTTTGCGTGTTATATATCATTAAAACGGTAATAGATTGACATTTGATTCTAATAA--CGTTCAAAACGCACAATATATAGTAATTTTGCCATTATCTAACTGTAAACTAAGATTATT-

FIG. 17B

- ATTGGATTTTTGTCACACTATTATATCGCTTGAAATACAATTGTTTAACATAAGTACCTG -
- TAACCTAAAAACAGTGTGATAATATAGCGAACTTTATGTTAACAAATTGTATTCATGGAC -
- TAGGATCGTACAGGTTTACGCAAGAAAATGGTTTGTTATAGTCGATTAATCGATTTGATT -
- ATCCTAGCATGTCCAAATGCGTTCTTTTACCAAACAATATCAGCTAATTAGCTAAACTAA
- -CTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGTTAACGCGTTGGAATTCGA-
- -GATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCAATTGCGCAACCTTAAGCT-

SacII

- -GCTCACTAGTGTCGACCTGCAGGGTACCATGGAAGCTTACTCGAGGATCCGCGGAAAGAA-
- CGAGTGATCACAGCTGGACGTCCCATGGTACCTTCGAATGAGCTCCTAGGCGCCTTTCTT -
- -GAAGAAGAAGAAGCCCGAAAGGAAGCTGAGTTGGCTGCCACCGCTGAGCAATA-
- CTTCTTCTTCTTCGGGCTTTCCTTCGACTCAACCGACGACGGTGGCGACTCGTTAT -
- ACTAGCATAACCCCTTGGGGCCTCTAAACGGGTCTTGAGGGGTTTTTTGCTGAAAGGAGG-
- -TGATCGTATTGGGGAACCCCGGAGATTTGCCCAGAACTCCCCAAAAAACGACTTTCCTCC-
- -AACCGCTCTTCACGCTCTTCACGC 3'
- -TTGGCGAGAAGTGCGAGAAGTG 5'

(<u>Sac</u>II sticky end)

(position #5904 in pAMG21)

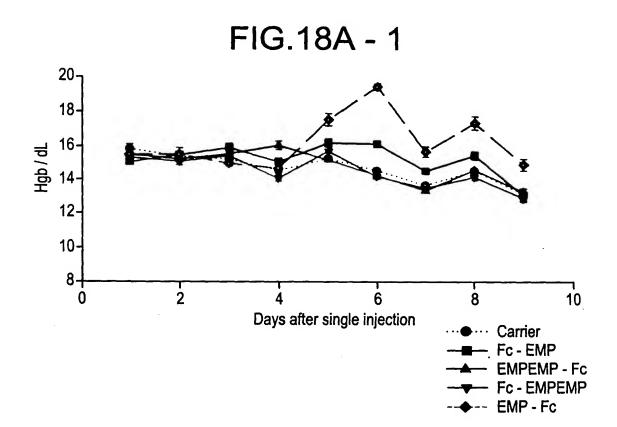


FIG.18A - 2

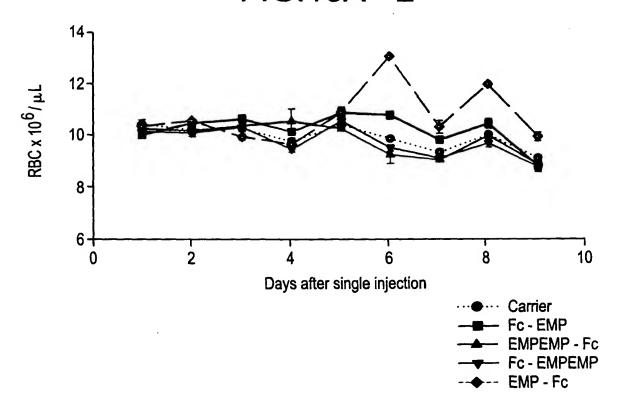


FIG.18A - 3

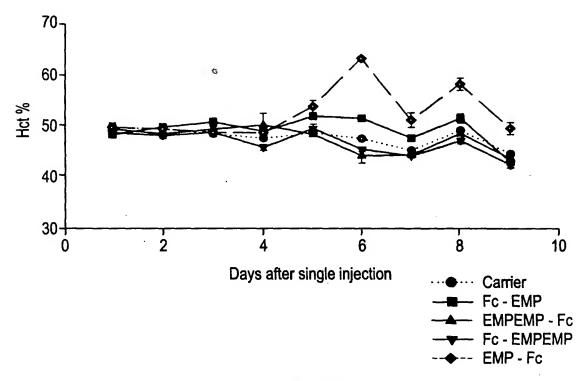


FIG.18B - 1

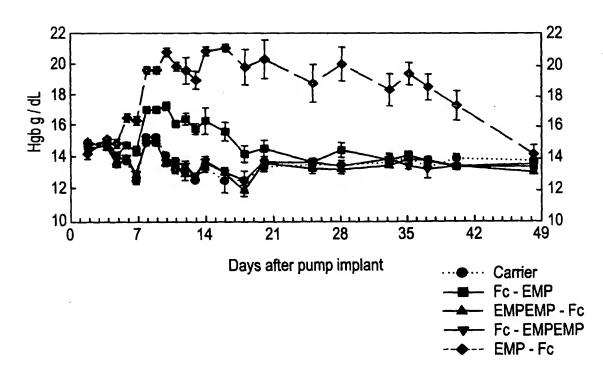


FIG.18B - 2

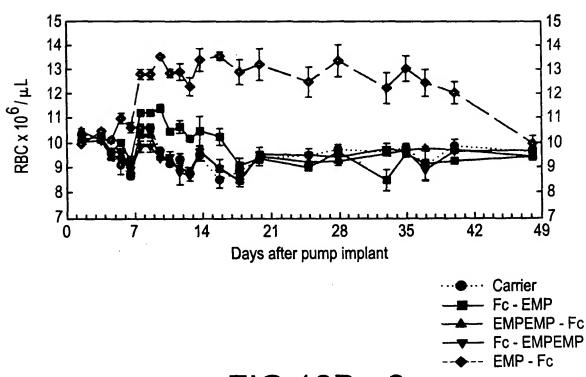
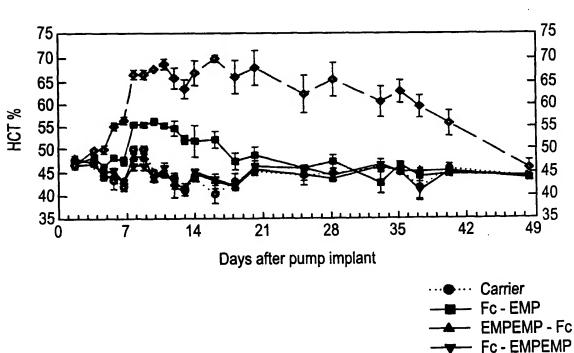


FIG.18B - 3



- EMP-Fc

TITLE: MODIFIED PEPTIDES AS THERAPEUTIC AGENTS

INVENTORS: FEIGE, et al. APPLN. NO: A-527D

a

FIG. 19A NdeI . CATATGGACAAAACTCACACATGTCCACCTTGTCCAGCTCCGGAACTCCTGGGGGGACCG GTATACCTGTTTTGAGTGTGTACAGGTGGAACAGGTCGAGGCCTTGAGGACCCCCTGGC a M D K T H T C P P C P A P E L L G G P TCAGTCTTCCTCTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG 61 ------ 120 AGTCAGAAGGAGAAGGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTC SVFLFPPKPKDTLMISRTPE a GTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTAC 121 -----+ 180 CAGTGTACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATG a V T C V V V D V S H E D P E V K F N W Y GTGGACGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGC CACCTGCCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCCTCCTCGTCATGTTGTCG V D G V E V H N A K T K P R E E Q Y N S a **ACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAG** TGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGACTTACCGTTCCTC T Y R V V S V L T V L H Q D W L N G K E a TACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAA 301 ------ 360 ATGTTCACGTTCCAGAGGTTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTT Y K C K V S N K A L P A P I E K T I S K a GCCAAAGGGCAGCCCGAGAACCACAGGTGTACACCCTGCCCCATCCCGGGATGAGCTG 420 CGGTTTCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGAC A K G Q P R E P Q V Y T L P P S R D E L a ACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCC 480 421 TGGTTCTTGGTCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGG TKNQVSLTCLVKGFYPSDIA a GTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG CACCTCACCCTCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGAC V E W E S N G Q P E N N Y K T T P P V L a GACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAG CTGAGGCTGCCGAGGAAGAAGGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTC D S D G S F F L Y S K L T V D K S R W Q

FIG. 19B

	601	CA	GGG	GAA	CGT -+-	CTT	CTC														GCAG	660
		GT	CCC	СТТ	GCA	GAA	GAG	TAC	GAG	GCA	CTA	CGT	ACT	'CCG	AGA	.CGI	GTI	GGT	GAT	GTG	CGTC	
a		Q	G	N	V	F	s	С	S	v	M	н	E	A	L	Н	N	Н	Y	T	Q	•
	661		GAG																		CTAC	
	001		CTC																		GATG	
a		K	3	L	S	L	S	P	G	K	G	G	G	G	G	D	F	L	P	Н	Y	•
											Ва	ımHI I										
	721				CTC										757	,						
	. = -	TT	TTT	GTG	GAG	AGA	CCC	AGT	GGC	AGG	CAT	TAC	CTA	\GG								
a		K	N	T	S	L	G	H	R	P	*											

FIG. 20A

		Nd	eI																		
		CAT	ATGG	ACTI	CCT	GCC	GCA	CTA	CAA	AAA	CAC	CTC	TCT	GGG	TCA	CCG'	TCC	GGG'	TGG	AGGC	
	1		racc'	rgaa	GGA	CGG	CGT	GAT	GTT	TTT	GTG	GAG	AGA	ccc	AGT	GGC	AGG	ccc.	ACC'	rccg	60
a		ı	M D	F	L	P	н	Y	K	N	T	S	L	G	Н	R	P	G	G	G	-
	61		GGGG/																		120
	.		ccc																		120
a		G (G D	К	T	н	T	С	P	P	С	P	A	P	E	L	L	G	G	P	•
	121		GTTT	+ -		• • •	+				+			-+-	· · ·		+			+	180
a			V F																P		
_			ACAT(-								-		_		_	
	181			+ -			+				+			-+-			+			+	240
a		v ·	т с	V	V	V	D	V	S	Н	E	D	P	E	V	K	F	N	W	Y	-
	241	· · ·	GACG CTGC	+-			+				+			-+-			+			+	300
a		v :	D G	v	E	v	н	N	A	К	T	ĸ	P	R	E	E	Q	Y	N	s	-
	301		TACC	+-			+				+			-+-			+	• • •		+	360
•			ATGG Y R		V	S	.GCA V		T.		L L		0	D	W		N N	ACC G	K	E	_
a	361	TAC.	AAGT(GCAA	GGI	CTC	CAA	CAA	AGC	CCT	ccc	AGC	ccc	CAT	CGA	GAA	AAC	CAT	CTC	CAAA	420
a			K C		v	s		K			P			I		ĸ		I	s	ĸ	
	421		AAAG TTTC	+ -			+	· • • •			+			-+-		• • •	+	• • •		+	480
a		A	K G	Q	P	R	E	P	Q	v	Y	T	L	P	P	S	R	D	E	L	
	481			+-			+				+			-+-			+			CGCC	540
																				GCGG	
a																				A	
	541			+-							+			-+-			+			GCTG + CGAC	600
a		٧	E W	E	s	N	G	Q	P	E	N	N	Y	К	T	T	P	P	V	L	

FIG. 20B

	601	• •	• • •	• • •	-+-			+				+			-+-			+			GCAG + CGTC	660
a		D	s	D	G	S	F	F	L	Y	s	ĸ	L	T	v	D	K	3	R	W	Q	•
	661				-+-			+				+			-+-			+			GCAG + CGTC	720
a		Q	G	N	v	F	S	С	s	V	M	Н	E	A	L	н	N	H	Y	T	Q	-
	721				CTC -+- GAG			+			ATA	+	GAT		-+-	76	1		•			
_		1.5		Ŧ	0	7	0	Ð	C	7	*											

FIG. 21A

	Ne	deI																				
	1	CAT	TAT	GGA	CAA.											GGA					ACCG	C 0
	_	GT	ATAC	CCT	GTT'																rggc	60
a			M	D	K	T	Н	T	С	P	P	С	P	A	P	E	L	L	G	G	Ð	•
	61		· - •		-+-			+				+			-+-		 .	+		• • •		120
•			CAC																_		ACTC	
a		S	V 13.07	F	L	F	P	P	K	P	K	D CC3	T	L	M	I	S	R	T	P	E	•
	121		• • •	· • • ·	- + -			+				+			-+-		· • • ·	+ -	.	• • • •	STAC + CATG	180
a		v	т	C	v	v	V.	D	v	s	н	E	ם	P	E	v	ĸ	F	N	W	Y	-
																					CAGC	
	181																				STCG	240
a		v .	D	G	V	E	V	н	N	A	K	T	ĸ	P	R	E	E	Q	Y	N	S	•
	241				+-		• • •	+				+			-+-			-+-	• • •	• • •	GGAG CCTC	300
a		T	Y	R	V	v	S	V	L	T	V	L	Н	Q	D	W	L	N	G	ĸ	E	-
	301				-+-			+		• • •		+		• • •	-+-	• • •		+	• • • ·			360
_												_				_			_		ettt 	
a		Y	K	C	K	V	S	N	K NGC	A	L CCM	P	A CRC	CCW/	I	E	K	T CC	I	S	K	•
	361				+-		· · ·	+				+	•	· - •	-+-			+	• • • •	• • •	GCTG + CGAC	420
a		A	K	G	Q	P	R	E	P	Q	V.	Y	т	L	P	P	s	R	D	E	L	
	421				+-	÷		+				+			- + -			+	• • • ·		GCC GCGG	480
a		T	ĸ	N	Q	V	s	L	T	С	L	v	K	G	F	Y	P	s	ם	I	A	-
	481			• • • •	+-			+				+			-+-	• • •	-,	+		·	GCTG + CGAC	540
a																					L	-
	541				- + -			+	• • •		• • •	+			-+-	• • •	• • •	+			GCAG + CGTC	600
a		D	s	D	G	s	F	F	L	Y	s	К	L	Т	v	D	K	s	R	W	Q	•

FIG. 21B

	601				-+-			+				+			-+-			+			GCAG + CGTC	660
a		Q	G	N	v		s		s			н				н		н		т	Q	
	661	- •			-+-			+				+	• • •		-+-			+	• • •		GGGT + CCCA	720
a		ĸ	S	L	s	L	S	P	G	K	G	G	G	G	G	F	E	W	T	P	G	-
											Ва	mHI i										
	721				-+-			• • •		GCT		+			-+-		763					
a		Y	W	Q	P	Y	Α	L	P	L	*											

FIG. 22A

		N	deI						•		- .			•								
			TAT	GTT												TCT	GCC	GCT	GGG	TGG.	AGGC	
	1	GT	ATA	CAA					CCC							AGA	CGG	CGA	CCC	ACC'	TCCG	60
a			M	F	E	W	T	P	G	Y	W	Q	P	Y	A	L	P	L	G	G	G	•
	61			• • •	-+-			+				+			-+-			+			ACCG	120
		CC	ACC	CCT	GTT'	TTG	AGT	GTG	TAC.	AGG	TGG	AAC	GGG	TCG	TGG	ACT	TGA	GGA	CCC	CCC'	TGGC	
a		G	G	D	K	T	Н	Т	С	P	P	С	P	A	P	E	L	L	G	G	P	•
	121				-+-			+				+			-+-			+			TGAG + ACTC	180
a		s	v	F.	L	F	P	P	к	P	к	D	т	L	M	r	s	R	T	P	E	
		GTO	CAC	ልጥርሪ	CGT	GGT	- GGT	GGA	CGT(- ദമദ	CCA	CGA	AGA	-		_			-	•	GTAC	
	181				- + -			+				+			-+-			+			+	240
_			31 G		JCA.										_					GAC	CATG	
a		V	Т	С	V	V	V	D	V	S	H	E	D	P		V	-	F	N	W	Y	•
	241				-+-			+				+•-	• • •		-+-			+			CAGC + GTCG	300
a			D		v		v	н	N				ĸ				E	0	Y	N	s	_
u					-	_			•			_						-	_		GGAG	
	301				-+-			+				+			-+-			+			+	360
					nca.	···		GCA							_						CCTC	
a		T	Y	R	· ·	v 	S 	v 	L	T	v 	L	Н	Q	D 	W	L	N	G	K	E	•
	361				-+-			+				+			-+-			+			CAAA	420
																					GTTT 	
a		Y	K	C	K	V	S	N	K	A	L	P	A	P	I	E	K	T	I	S	ĸ	•
	421				-+-			+				+	• - • ,		-+-	• • •		+				480
		CG	GTT'	rcc	CGT	CGG	GGC	TCT	TGG'	TGT	CCA	CAT	GTG	GGA	CGG	GGG	TAG	GGC	CCT	ACT	CGAC	
a		A	K	G	Q	P	R	E	P	Q	V	Y	T	L	P	P	S	R	D	E	L	•
	481																		CGA	CAT	CGCC	540
	401																		GCT	GTA	GCGG	
a		T	ĸ	N	Q	v	S	L	T	С	L	V	K	G	F	Y	P	s	D	I	A	-
	541.	GT	GAG	GTG	GGA	GAG	CAA	TGG	GCA	GCC	GGA	GAA	CAA	CTA	CAA	GAC	CAC	GCC	TCC	CGT	GCTG	600
	341																				CGAC	500
a		v	E	W	E	s	N	G	Q	P	E	N	N	Y	K	T	T	P	P	v	L	•

FIG. 22B

	601				-+-			+			• • •	+			-+-			+			GCAG + CGTC	660
a		D	s	D	G	s	F	F	L	Y	s	ĸ	L	T	Å	D	K	s	R	W	Q	•
	661			• • •	-+-			+				+			-+-			+			GCAG + CGTC	720
a		Q	G	N	V	F	S	С	s	V	M	Н	E	A	L	Н	N	н	Y	T	Q	-
											Ва	IHm. I										
	721		GAG CTC		.+-			+				+			757	1			•			
а		к	S	L	s	L	s	P	G	к	*											

FIG. 23A

	No	leĮ																				
	1			· ·	-+-			+				+		·	-+		· ·	+ -		· -		60
		GTA	TAC	CCT	GTT?	rtg.	AGT	GTG'	TAC	AGG'	rgg	CAC	GGC	rcgi	rgga	CTI	'GAC	GAC	CCC	CCI	'GGC	
a			M	D	K	Т	Н	Т	С	P	P	С	P	A	P	E	L	L	G	G	₽	•
	61				-+-			+				+		 .	+			-+-			CTC	120
a		S	v	F	L	F	P	Þ	ĸ	P	ĸ	D	т	L	M	I	s	R	T	P	Ε.	
	121-				-+-			+	• • •			+			+			+	• • •		GTAC CATG	180
a		v	T	С	V	V	v	a	v	s	Н	E	D	P	E	V	ĸ	F	N	W	Y	•
	181				-+-	• • •		+				+		• • •	-+-			+		• • • •	CAGC + GTCG	240
a		V	D	G	v	E	v	н	N	A	ĸ	T	K	P.	R	E	E	Q	Y	N	s	•
	241				-+-			+				+			-+-			+	• • •	· · · ·	GGAG CCTC	300
a		T	Y	R	v	v	s	v	L	T	v	L	н	Q	D	W	L	N	G	K	E	•
	301				- + -			+				+			-+-			+			CAAA GTTT	360
a		Y	K	С	K	V	S	N	K	A	Ļ	P	A	P	I	E	K	T	I	S	K	•
	361				-+-			+				+			-+-			+		• • •	GCTG + CGAC	420
a		A	K	G	Q	P	R	E	P	Q	V	Y	T	L	P	P	S	R	D	E	L	•
	421				-+-			+				+			-+-			+			CGCC + GCGG	480
a		T	ĸ	N	Q	V	s	L	T	C	L	v	ĸ	G	F	Y	P	S	D	I	A	•
	481				-+-			+				+			-+-			+			GCTG + CGAC	540
a		v	E	W	E	S	N	G	Q	P	E	N	N	Y	ĸ	T	T	P	P	V	L	-
	541				-+-			+				+			-+-			+			GCAG + CGTC	600
a		D	s	D	G	S	F	F	L	Y	s	K	L	T	v	D	K	s	R	W	Q	•

FIG. 23B

	601				-+-			+				+ - •			-+-			+			GCAG + CGTC	660
a		Q	G	N	V	F	S	C	s	V	M	Н	E	A	L	Н	N	Н	Y	T	Q	
	661				-+-			+	• • •			+			-+-			+			TGAC + ACTG	720
a		K	S	L	s	L	s	P	G	ĸ	G	G	G	G	G	V	E	P	N	С	D	•
	721				TAT -+- ATA		• • •	+				+			-+-	ACT		GGA		77	3	
a		I	н	v	M	W	E	W	E	С	F	E	R	L	*							

FIG. 24A

	No	leI																				
	1		· ·		-+-		- 	+		· · ·		TGT'			-+-	·		+ -	·		+	60
_		GTA																			GCA	
a			M	V 	E	P	N	С 	D	I	Н	V	M	W	E	W 	E	C	F	E	R	•
	61		 .		- + -			+				+			-+-			+ -			CTC + 'GAG	120
a		L	G	G	G	G	G	D	K	T	н	т	С	P	P	С	P	A	p	E	L	-
	121		·		- + -			+				+	• • •		-+-			+ -			TCC SAGG	180
a		L	G	G	P	s	v	F	L	F	P	P	ĸ	P	K	D	T	L	M	I	S	-
	181		 .		-+-	- 		+				+			-+-			+	• • • •		AAG TTC	240
a		R	т	P	E	v	T	С	v	v	v	D	v	S	H	E	D	P	E	V	K	•
	241				-+-			+				+		· · ·	-+-			+ -	·		GAG + CCTC	300
a		F	N	W	Y	V	D	G	V	E	V	H	N	A	K	T	K	P	R	E	E	•
	301				-+-			+				+			-+-			+			GCTG	360
a		Q	Y	N	S	T	Y	R	V	V	S	V	L	T	V	L	Н	Q	D	W	L	•
	361				-+-			+				+			-+-			+			GAAA CTTT	420
a		N	G	K	E	Y	K	С	K	V	S	N	K	A	L	P	A	P	I	E	K	•
	421				-+-			+				+		• • •	-+-			+		•	ATCC + ragg	480
a		T	I	S	K	A	K	G	Q	P	R	E	P	Q	V	Y	T	L	P	P	S	-
	481	GC	CCT	ACT	-+- CGA	CTG	GTT	+ CTT	GGT	CCA	GTC	+	CTG	GAC	-+- GGA	CCA	GTT	TCC	GAA	GAT	AGGG	540
a																					P	•
	541	TC	GCT	GTA	- + - GCG	GCA	CCT	CAC	CCT	CTC	GTT	ACC	CGT	CGG	CCT	CTT	GTT	GAT	GTT	CTG	CACG + GTGC	600
a		S	D	I	A	V	E	W	E	S	N	G	Q	P	E	N	N	Y	K	T	T	•

FIG. 24B

	601			• • •	-+-			+				+			-+-			+		• • •	CAAG + GTTC	660
a		P	P	V	L	D	S	D	G	s	F	F	L	Y	S	K	. L	T	v	а	ĸ	-
	661		• • •		-+-	• • •		+	• • •			+		• • •	-+-	• • •	• • •	+	•••		CAAC + GTTG	720
a		s	R	W	Q`	Q	G	N	V	F	s	С	S	V	M	H	E	A	L	н	N	•
													÷			В	amH	I				
	721				-+-			+		GGA		+			-+-			+		77	3	
a		н	Y	T	Q	K	s	L	S	L	s	P	G	K	*							

FIG. 25A

	No	deļ																				
	1	CAT	TAT	GGA(CAA			CAC								GGA	ACT		_		ACCG	60
		GT	\TA	CCT	GTT'	TTG	AGT	GTG	TAC	AGG	TGG	AAC	AGG	TCG.	AGG	CCT'	rga(GGA	CCC	CCT	rggc	30
a			M	D	K	T	н	T	С	P	P	C	P	A	P	E	L	L	G	G	P	•
	61	TC														GAT	CTC	CCG	GAC	CCC	rgag	
	01															CTA	GAG	GGC	CTG	GG.	ACTC	120
a		s	V	F	L	F	P	P	ĸ	P	ĸ	D	T	L	M	I	s	R	т	P	E	-
	121				-+-			+			·	+			-+-	• • •		+			GTAC + CATG	180
a		v	ጥ	С				ם					_			v					Y	_
		cme	-		٠		·			-	,			-				_		••	-	•
	181				-+-			+				+			-+-			+				240
																					GTCG	
a		V	D	G	V	E	V	н	N	A	K	Т	K	P	R	E	E	Q	Y	N	S	•
	241				-+-			+				+			-+			+			GGAG + CCTC	300
a		T	Y	R	v	v	S	v	L	T	v	L	н	Q	D ·	W	L	N	G	ĸ	E	•
	301				-+-			+			· · ·	+			-+-			+			CAAA GTTT	360
a		Y	K	С	K	v	s	N	ĸ	A	L	P	A	P	I	E	K	T	I	s	ĸ	-
	361				-+-			+				+			-+-			+			GCTG + CGAC	420
a		A	ĸ	G	Q	P	R	E	P	Q	v	Y	T	L	P	P	s	R	D	E	L	-
	421				-+-		• • •	+				+	• • •		-+-			+			GGCC + GCGG	480
a																					A	
u					_																GCTG	
	481				-+-			+				+		· · ·	-+-			+			CGAC	540
a		v	E	W	E	8	N	G	Q	P	E	N	N	Y	K	T	T	P	P	V	L	-
	541				-+-			+				+			-+-			+			GCAG	600
																					CGTC	_
2		13	~	1.1	(2		100	-	1.4	¥	-	ĸ		.1.	~	u	~	3	~	44	~	-

FIG. 25B

	601				-+-			+				+			-+-			+			GCAG + CGTC	660
1		Q	G	N	v	F	s	C _.	s	v	M	н	E	A	L	н	N	н	Y	T	Q	-
	661				-+-			+				+			-+-			+			GGGT	
1		ĸ	s	L	Š	L	3	P	G	K.	G	G	G	G	G	С	T	T	H	W	G	-
	721		• • •		-+-	CT.	IMMI ATC	GAT			·	748										
		177	d)	Т.	C	*																

FIG. 26A

	No	leI																				
	1		• • •		- + -			+		- • •		+			-+-		 .	+	AGGT	60
		GT	ATA	CAC	GTG	GTG	GGT	GAC	CCC	AAA	GTG	GGA	CAC	GCC	ACC'	rcco	GCC1	ACC	CTC	GTT?	CCA	
à			M	С	T	T	Н	W	G	F	T	L	С	G	G	G	G	G	Ø	ĸ	G	-
	61	GG/	AGG	CGG'	TGG	GGA	CAA		TCA										ACTO	CTC	GGG	120
	01	CC	rcc	GCC.	ACC	CCT	GTT												rgac	GAC	ccc	120
a		G	G	G	G	D	K	T	H	T	С	P	P	С	P	A	P	E	L	L	G	•
	121				-+-			+				+			-+-			+			GACC + CTGG	180
3		G	P	s	v	F	L	F	P	P	K	P	K	D	T	L	M	I	3	R	T	•
		CC	rga(GGT	CAC	ATG	CGT	GGT	GGT	GGA	CGT	GAG	CCA	CGA	AGA	ccc	TGA	GGT	CAAC	GTT	CAAC	
	181								CCA									-			GTTG	240
a		P	E	v	т	С	v	v	v	D	v	s	н	E	ם	P	E	v	ĸ	F	N	
-		TGO	מחב	ርርጥ	CC A	നമര	උርጥ	CGA	CGTP:	GC A	י. ממידי					_		Grac	GGA(CA(GTAC	
	241				-+-		• • •	+				+			-+-			+			CATG	300
		W	Y	V		G	v	E	v	H.	N N	ACG A	K	т	ĸ	P	R	E	E	0	Y	_
•		.,	-			_		_	•					_		-			_	-	rGGC	
	301				-+-			+				+			-+-			+			ACCG	360
a		N	s	ого Т	Y	R	v	v	s	v	L	т	v	L	н	0	ם	w	L	N	G	
a				-			·	•	_	•		_	•	_		-	_	•	_		CATC	
	361				-+-			+				+			-+-			+			GTAG	420
																_	_			_	_	
3.		K	E	Y	K	C	K	V	_	N		A		P	A 	P 	I	e	K	T	I	•
	421				-+-			+			•	+			-+-			+			GGAT	480
																					CCTA	
a																					D	
	481				-+-			+				+			-+-			+			CGAC + GCTG	540
a																					D	-
-		ልጥር	CGC	CGT	GGA	GTG	GGA	GAG	CAA	TGG	GCA	GCC	GGA	GAA	CAA	CTA	CAA	GAC	CAC	GCC'	TCCC	
	541				-+-			+				+			-+-			+			AGGG	600
a		I	A	v	E	W	E	S	N	G	Q	P	E	N	N	Y	K	T	T	P	P	-

FIG. 26B

	601	• •			-+-	• • •	-	+				+		• • •	-+-			+				660
		CA	CGA	CCT	GAG	GCT	GCC									GTG	GCA	CCT	GTT		GTCC	
a		V	·L	D	S	D	G	S	F	F	L	Y	S	K	L	T	٧	D	K	S	R	-
	661	TG	GCA	GCA	GGG -+-	GAA	CGT														CTAC	720
		AC	CGT	CGT	CCC	CTT	GCA	GAA	GAG	TAC	GAG	GCA	CTA	CGT	ACT	CCG	AGA	CGT	GTT	GGT	GATG	r
a		W	Q	Q	Ģ	N	V	F	S	C	3	V	M	Н	E	A	L	Н	N	Н	Y	•
		•											Ва	I Hou								
	721				-+-	CCT GGA		+				+			-+-		763	i	•			
a		т	Q	ĸ	s	L	s	L	s	P	G	K	*									